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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,458	ANDERSON ET AL.	
	Examiner	Art Unit	
	S. DEVI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-9,33-36 and 38-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7-9,33-35 and 38-54* is/are rejected.

7)☒ Claim(s) *5, 6 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/20/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Prosecution Reopened

1) In view of Applicants' Information Disclosure Statement filed on 01/20/11, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

Information Disclosure Statement

2) Acknowledgment is made of Applicants' Information Disclosure Statement filed 01/20/11. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Applicants' Reply Brief

3) Acknowledgment is made of Applicants' reply brief filed 01/10/11.

Status of Claims

4) Claims 1, 4-9, 33-36 and 38-54 are pending and are under examination.

Rejection(s) under 35 U.S.C. § 102

5) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6) Claims 1, 4, 7, 33 and 49 are rejected under 35 U.S.C. § 102(a) as being anticipated by Roche et al. (Microbiology 149: 643-654, March 2003 – Applicants' IDS) as evidenced by the IDS document 'Opposition against European Patent No. 1651166 in the name of Merck Sharp & Dogme Corp. – Applicants' IDS) and Applicants' admitted state of the prior art.

Roche et al. taught a purified recombinant N-terminal truncate of SasJ protein composition (i.e., ORF0657) of S. aureus, referred to as SasJ48-477, which reacted specifically with antibodies in convalescent sera from patients with S. aureus infections. Roche et al. taught of the suitability of LPXTG-anchored surface proteins of S. aureus (SasJ included) for the development of vaccines against S. aureus. See Table 1 and pages 645, 649 and 652. That the prior art SasJ polypeptide has at least 94% identity with the instantly recited SEQ ID NO: 3 and that Roche's purified SasJ48-477 fragment has at least 94% identity with the instantly claimed SEQ ID NO: 1 of the instant claims is inherent from the teachings of Roche et al. in light of what was known to those of skill in the art. For example, the Applicant-submitted IDS document 'Opposition against European Patent No. 1651166 in the name of Merck Sharp & Dogme Corp.

indicates that Roche's polypeptide fragment containing amino acids 48-477 of SasJ (ORF0645) shares at least 94% amino acid identity with SEQ ID NO: 1. See page 7. Furthermore, Applicants themselves acknowledge in the instant specification the following to be known in the art. Applicants' specification acknowledges that ORF0657n sequence is given different designations in the art including the designation, SasJ. See first full paragraph under Example 4 or on page 27 of Applicants' specification. Thus, Roche's purified SasJ48-477 fragment is from the admittedly art-known SasJ polypeptide. Since the prior art product meets the structural limitations of the claims, it is expected to necessarily possess the same function(s) as that of the instantly claimed product, i.e., the capacity to provide protective immunity against S. aureus, or the capacity to be an immunogen as defined at line 25 of page 2 of Applicants' specification. Note that '[p]roducts of identical chemical composition can not have mutually exclusive properties.' A chemical product and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicants disclose in the specification and/or claims, i.e., provide protective immunity against S. aureus, or the capacity to be an immunogen as defined at line 25 of page 2 of Applicants' specification, are necessarily present.

Claims 1, 4, 7, 33 and 49 are anticipated by Roche et al.

Rejection(s) under 35 U.S.C § 103

7) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

8) Claims 8, 9 and 38-40 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Roche et al. (Microbiology 149: 643-654, March 2003 – Applicants' IDS) in view of Foster et al. (US 2003/0186275 A1) ('275).

The teachings of Roche et al. are explained above which do not expressly teach the presence of a pharmaceutically acceptable carrier and/or an adjuvant along with their purified SasJ48-477 composition.

However, adding an art-known pharmaceutically acceptable carrier and/or an art-known adjuvant to a prior art polypeptide composition was routine and conventionally practiced in the art at the time of the invention. For example, Foster et al. ('275) disclosed having a carrier and/or an adjuvant in a polypeptide immunogen-containing vaccine composition against S. aureus. See paragraphs [0055] to [0064].

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to add an art-known pharmaceutically acceptable carrier and/or an art-known adjuvant as taught by Foster et al. ('275) to Roche's purified polypeptide composition that was already demonstrated in the art to react specifically with antibodies in convalescent sera from patients with S. aureus infections, to produce the instant invention, since it was routine and

conventional in the art of polypeptide immunogens or vaccines to add an art-known pharmaceutically acceptable carrier and/or an art-known adjuvant thereto for the purpose of using the polypeptide as a vaccine candidate and/or for improving its immunogenicity.

Claims 8, 9 and 38-40 are prima facie obvious over the prior art of record.

Rejection(s) Maintained

9) The rejection of claim 8 made in paragraph 25(f) of the Office Action mailed 11/24/09 and maintained in paragraph 16 of the Office Action mailed 03/25/10 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein. Applicants' arguments in the reply brief are repetitive and have already been addressed in the Advisory Action and the Examiner's Answer.

10) The rejection of claim 7 made in paragraph 25(g) of the Office Action mailed 11/24/09 and maintained in paragraph 17 of the Office Action mailed 03/25/10 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein.

Applicants contend that claim 7 indicates the additional region or moiety being joined to an immunogen 'comprising' an amino acid sequence at least 90% identical to SEQ ID NO: 1 and the reference to amino acid sequence provides for a polypeptide. Applicants state that the skilled artisan reading claim 7 would readily understand the additional region or moiety facilitates stability of the polypeptide it is attached to, which is the only amino acid sequence specifically recited as present. Applicants cite case law and submit that definiteness under 35 U.S.C. 112, second paragraph, is determined based on whether those skilled in the art would understand what is claimed when the claim is read in light of the specification.

Applicants' arguments have been considered, but are not persuasive.

Unlike claim 1, the immunogen claimed in claim 7 is not a 'purified polypeptide' immunogen. The reference to an amino acid sequence in line 1 of the claim provides for the non-purified immunogen, which can have a dipeptide sequence impurity, a dipeptide sequence linker, or an extraneous polypeptide sequence attached thereto. Claim 7 continues to be vague and indefinite in the limitation: 'facilitates polypeptide stability', because it is unclear the stability of which polypeptide is being facilitated by the one or more additional regions or moieties. The claim has no earlier recitation of any 'polypeptide'. The claimed immunogen is not purified and is expected to contain extraneous polypeptides in major or residual amounts. It is unclear the stability of which polypeptide is facilitated. Is the 'polypeptide' whose stability is facilitated, a contaminant polypeptide or a residual impurity that is associated with the claimed immunogen? The relationship to the claimed immunogen, if any, of the polypeptide whose stability is facilitated, is not understood. The rejection stands.

11) The rejection of claims 9 and 38-54 made in paragraph 25(i) of the Office Action mailed 11/24/09 and maintained in paragraph 18 of the Office Action mailed 03/25/10 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein.

12) The rejection of claims 1, 4, 7-9, 33-35, 38-44 and 49-51 made in paragraph 23 of the Office Action mailed 11/24/09 and maintained in paragraph 15 of the Office Action mailed 03/25/10 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is maintained for the reasons set forth therein and reemphasized herein below.

Most of the arguments presented in Applicants' reply brief filed 01/10/11 on this rejection have already been addressed previously in the Advisory Action mailed 03/25/10 and the Examiner's Answer mailed 11/10/10.

Applicants state that the Office is incorrect in assuming that conformational 'epitomes' are present. However, neither the Examiner's Answer nor any other previous Office Action, made a mention of 'epitomes', let alone asserted the presence of 'conformational epitomes'.

Applicants further state that 'SEQ ID NO: 28 antigen does not induce "cell death", as asserted by the Office'. However, the Examiner's Answer did not include the phrase 'cell death' either as such or in connection with SEQ ID NO: 28.

With regard to the Office's documentation of Applicants' SEQ ID NO: 28 (i.e., the His-tagged full length SEQ ID NO: 2) not being able to provide approximately 80% protection via survival among mice immunized therewith followed by challenge with one of CL-10, CL-13 and CL-18 (Figures 4A, 4D and 4G), Applicants state the following:

> The Office correctly acknowledges that based on the ability of the longer-length SEQ ID NO: 28 sequence to provide protection against a S. aureus challenge strain, the skilled artisan would have expectations concerning the ability of the ORF0657nI region present in the challenge strain to provide protection against S. aureus.

However, what was documented in the Examiner's Answer with regard to Applicants' SEQ ID NO: 28 not being representative of the claimed broad genus, was the following:

> It is important to note that the percent identity recited in the instant claims covering the elected species is relative to SEQ ID NO: 1, and is not relative to SEQ ID NO: 2 and is not relative to SEQ ID NO: 28.
>
> The amino acid sequence of SEQ ID NO: 2, comprising therein the SEQ ID NO: 1 without its amino terminal methionine, is the full-length COL ORF0657n polypeptide. The full-length polypeptide was known in the art at the time of the invention as taught by Foster et al. (US

6,841,154). See the art rejection made at paragraph 14 of the Office Action mailed 12/15/08. Appellants have expressly acknowledged previously that the full-length ORF0657n sequence is excluded from the claimed invention. For example, at third full paragraph on page 9 of the amendment/remarks filed 08/18/08, Appellants stated the following [Emphasis added]:

> 'Claim 1 **excludes** SEQ ID NO: 2'.

Again, at first full paragraph on page 20 of Applicants' amendment/remarks filed 03/13/09, Appellants stated the following [Emphasis added]:

> Claims 1, 5, 7, and 8 were amended as discussed above, so that **the full-length ORF0657n sequence is not covered**. Claims 3, 4, 6, 7, 33-35, and 37-44 as previously presented provided for less than the full-length sequence.

Thus, by Appellant's own admission, SEQ ID NO: 2 is not covered by the independent claims 1, 7 and 8.

With regard to Applicants' argument of SEQ ID NO: 28 being representative of the claimed broad genus of at least 90% or at least 94% identical polypeptide immunogen variants, the following must be noted. First, the percent identity recited in the instant claims is relative to SEQ ID NO: 1, not relative to SEQ ID NO: 28. The rejection of record is pertinent to polypeptide immunogen variants having up to 6% and 10% variations, substitutions, or modifications within an amino acid sequence consisting of SEQ ID NO: 1, with or without additional moieties either at the amino terminus or at the carboxyl terminus. The SEQ ID NO: 28 on the other hand is the His-tagged full-length SEQ ID NO: 2 containing an amino acid sequence that is 99.8% identical to SEQ ID NO: 1 plus additional amino acids, not only at the amino terminus, but also at the carboxyl terminus of SEQ ID NO: 1. See Figures 1B and 1C and Appellants' evidence Exhibit 1 or Appendix A. Accordingly, since SEQ ID NO: 2 itself is excluded from the scope of the instant claims (see Appellants' statement supra), SEQ ID NO: 28 of the instant specification, which is longer than SEQ ID NO: 2, is also excluded from the scope of claims 1 and 8 as well as claim 7. Furthermore, as Appellants have acknowledged previously, the ORF0657nI region of SEQ ID NO: 1 that overlaps with a portion of SEQ ID NO: 28 is 78% of SEQ ID NO: 28. See second paragraph on page 11 of Appellants' amendment/remarks filed 02/24/2010. Additionally, SEQ ID NO: 28, SEQ ID NO: 2, and the sequences depicted in Figures 2A-2E other than SEQ ID NO: 1 and 5, are not a fragment of a polypeptide immunogen consisting of SEQ ID NO: 3 or a fragment of a polypeptide immunogen consisting of an at least 94% identical variant of SEQ ID NO: 3. SEQ ID NO: 28 comprises a polypeptide that is 99.8% identical to SEQ ID NO: 1 with a single amino acid addition at the amino terminus of SEQ ID NO: 1 after methionine, but does not fall within the scope of the instant claims because it contains additional amino acids both at the amino and carboxyl termini of SEQ ID NO: 1. SEQ ID NO: 28 does not comprise, let alone consist of, an amino acid sequence variant that is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99.0% identical to SEQ ID NO: 1, or such an amino acid sequence variant differing from SEQ ID NO: 1 by up to 5, 10 or 25 amino acid alterations. Furthermore, the ORF0657nI-equivalent region of SEQ ID NO: 2 or SEQ ID NO: 28 does not constitute a 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99.0% identical variant species of an amino acid sequence consisting of SEQ ID NO: 1, when sequence identity is determined using an art-recognized algorithm. Therefore, SEQ ID NO: 28 and SEQ ID NO: 2 do not fall within the scope of the instant claims.

With regard to Appellants' argument on the longer-length polypeptide SEQ ID NO: 28 being representative of the claimed broad genus and its alleged ability to provide heterologous protection, the protection experiment results from Figure 4 must be noted. The experiments showing the alleged heterologous protection were all performed by administering SEQ ID NO: 28, which is a His-tagged SEQ ID NO: 2 and is not an immunogen consisting of an amino acid sequence 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 1 and differing from SEQ ID NO: 1 by up to 5, 10, or 25 alterations, and/or containing one or more additional regions or moieties covalently linked to said sequence at either the carboxyl or the amino terminus. The SEQ ID NO: 28 polypeptide, upon administration to mice in an immune-sufficient mouse model of S. aureus infection, induced approximately 80% death (not 80% survival) of the animals immunized therewith, following challenge infection with one of the three different clinical isolates of S. aureus, CL-10, CL-13, and CL-18. See Figure 4A, 4D and 4G. The SEQ ID NO: 28 polypeptide showed a death rate almost equal to the one induced in control mice immunized with the AHP adjuvant alone. See Figure 4A. Accordingly, a longer than full-length polypeptide causing about 80% death of the immunized mice or showing a death rate almost equal to the one induced in control mice immunized with an adjuvant alone, is not viewed by those of skill in the art as a polypeptide immunogen conferring protection to heterologous isolates of S. aureus and as a polypeptide immunogen representative of the claimed broad genus of protective polypeptide or immunogen variants.

Applicants further allege that the Office makes no mention of the difference in survival rates at days 5, 6 and 7.

However, it is the Applicants' specification, and not the Office, which sets forth the monitoring period of immunized and control mice. See line 29 of page 26 of the specification. The mice survival at the end of the experiment was the criteria used for determining protection in the instant application. For example, Example 3 is entitled: Protection Studies Using His-tagged ORF0657n Related Polypeptides. The experiment therein was set up such that the mice immunized with SEQ ID NO: 28 were challenged intravenously and monitored over a 14 day period for survival (FIG. 3A). '**At the end of the experiment,**' 11 mice survived the ORF0657n immunized group compared to three surviving in the AHP control group. See lines 29-31 of page 26 of the specification. Thus, the description of the mouse survival experiments in Applicants' specification required taking into account mice survival 'at the end of the experiment'. Thus, mice survival at the end of the experiment, but not at any desired generic point of time, was the criteria

used for determining protection. Example 6 also expressly states that the immunized mice were monitored for 10 days.

Furthermore, even if one takes into account the alleged difference in survival rates at days 5, 6 and 7 from all panels of Figure 4 and Figure 3A, these data are **not** representative of protection conferred by the claimed genus of polypeptide or immunogen fragments and variants, because SEQ ID NO: 2 contained within SEQ ID NO: 28, by Applicants' own admission is **excluded** from the scope of the instant claims as documented supra. SEQ ID NO: 28 is not a polypeptide or an immunogen consisting of an amino acid sequence 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99.0% identical to SEQ ID NO: 3 or SEQ ID NO: 1, and is not a fragment of SEQ ID NO: 3 comprising an amino acid sequence 94%, 95%, 96%, 97%, 98%, or 99.0% identical to SEQ ID NO: 1 capable of providing protective immunity against S. aureus.

In sum, SEQ ID NO: 28, i.e., His-tagged full length SEQ ID NO: 2, is '**not** covered by claims 1, 5, 7 and 8' as expressly acknowledged by Applicants. Furthermore, 'Claim 1 **excludes** SEQ ID NO: 2' as expressly acknowledged by Applicants, and therefore the His-tagged full length SEQ ID NO: 2, i.e., SEQ ID NO: 28, is also excluded from the scope of claim 1. Accordingly,

(A) SEQ ID NO: 28 is **not** representative of the claimed broad genus of protective polypeptide or immunogen fragments and variants.

(B) The alleged protection induced by SEQ ID NO: 28 as depicted in Figures 4 and 3A is **not** relevant to the requisite protective function of the claimed broad genus of polypeptide variants which **consist** of a fragment of an amino acid sequence up to 6% non-identical to SEQ ID NO: 3 and an amino acid sequence up to 6% non-identical to SEQ

ID NO: 1 and differing from SEQ ID NO: 1 by up to 25 amino acid alterations, or the claimed broad genus of immunogen variants **consisting** of an amino acid sequence up to 10% non-identical to SEQ ID NO: 1 as recited in claim 7 and differing from SEQ ID NO: 1 by up to 25 amino acid alterations.

(C) The full-length SEQ ID NO: 2 polypeptide comprised within SEQ ID NO: 28 comprises 2-446 amino acids of SEQ ID NO: 1 plus a very lengthy amino acid sequence at the carboxy terminus of 2-446 amino acids of SEQ ID NO: 1 and an amino acid sequence containing 42 additional amino acids at the N-terminus of 2-446 amino acids of SEQ ID NO: 1. The alleged protection induced by SEQ ID NO: 28 against CL-10, CL-13, CL-20, CL-18 and CL-21 has not been correlated to the sequence within SEQ ID NO: 28 that consists of 2-446 amino acids of SEQ ID NO: 1 with up to 25 amino acid alterations therein. Therefore, one or more epitopes from regions outside of 2-446 amino acids of SEQ ID NO: 1 within SEQ ID NO: 28 being potentially responsible for the alleged protection against CL-10, CL-13, CL-20, CL-18 and CL-21 has not been excluded or ruled out.

Applicants further contend that the ORF0657nI fragment 2 depicted in Figure 1 having about 91% sequence identity to SEQ ID NO: 1 is functionally excluded from claim 7. This issue was also addressed in the Examiner's Answer as indicated below:

> The immunogen claimed in the independent claim 7 is minimally required to (A) consist of an amino acid sequence 90% identical to SEQ ID NO: 1 (i.e., 10% non-identical) and one or more additional regions covalently joined thereto either at the carboxyl or the amino terminus as recited therein, facilitating the stability of an unspecified polypeptide; and (B) provide protective immune response against S. aureus. Although claim 7 does not include the recitation of providing 'protective immune response against S. aureus', the limitation 'immunogen' as defined

at line 25 of page 2 of Appellants' specification is required to have the ability to provide protective immunity, consistent with the intended prophylactic (i.e., vaccine) applications. Specifically, at line 25 of page 2 of the specification, Appellants expressly state that the following:

> Reference to "immunogen" indicates the ability to provide protective immunity.

Claims are interpreted in light of the specification. USPTO personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. Where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim. Toro Co. v. White Consolidated Industries Inc., 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999) (meaning of words used in a claim is not construed in a "lexicographic vacuum, but in the context of the specification and drawings."). With particular regard to the claim language used in the instant claim 7, the paragraph bridging pages 2 and 3 of Appellants' specification states the following [Emphasis added]:

> Another aspect of the present invention describes **an immunogen comprising an amino acid sequence that provides protective immunity against S. aureus**. The immunogen comprises an amino acid sequence at least 90% identical to SEQ ID NO: 1 and one or more additional regions or moieties covalently joined at the carboxyl terminus or amino terminus, wherein each region or moiety is independently selected from a region or moiety having at least one of the following properties: enhances the immune response, facilitates purification, or facilitates polypeptide stability.

Therefore, the immunogen claimed in the independent claim 7 is required by definition to provide protective immunity against S. aureus. The at least 90% identical immunogen claimed in the dependent claims 49-51 encompass those that differ from SEQ ID NO: 1 by up to 25, 20 or 5 amino acid alterations, and are still required to provide protective immunity against S. aureus as required by Appellants' express definition of the limitation 'immunogen'. See supra. Appellants' current argument that the immunogen of claim 7 is not associated with the protective function is contrary to the express definition provided in the as-filed specification.

Applicants further allege that the Office provides no basis for the necessity of retaining all amino acids of SEQ ID NO: 1 except the N-terminal methionine for retention of the protective function. However, the Examiner's Answer provided a detailed rationale and basis as reproduced below:

> Particularly noteworthy in this regard are the mouse protection results obtained with two specific fragments of SEQ ID NO: 1 as illustrated via Figure 1A. Appellants' SEQ ID NO: 1 when modified with specific known amino acid alterations by merely deleting amino acids 2-41 from its amino terminus, **did loose** its ability to provide protective immunity against a strain of S. aureus, despite retaining up to 91% sequence identity to SEQ ID NO: 1. The instant application at third full paragraph of page 8 states that a fragment of SEQ ID NO: 2 consisting of amino acids 82-486 and a fragment of SEQ ID NO: 2 consisting of 42-196 were **not protective**. See fragments 2 and 3 identified in Figure 1A and the brief description of the drawing for Figure 1A on page 5 of Appellants' specification. The amino acid residues 42-486 of SEQ ID NO: 2 constitute the full-length SEQ ID NO 1. The sequence consisting of the amino acids 82-486 of SEQ ID NO: 2 is

fragment 2 of SEQ ID NO: 1 and has as high as 91% structural identity to SEQ ID NO: 1 and falls fully within the scope of claim 7 sequence identity-wise. This fragment 2 however has been definitively correlated by Appellants to the lack of protective function against S. aureus. See third full paragraph of page 8; fragment 2 in Figure 1A; and the brief description of the drawing for Figure 1A. Appellants have reemphasized this lack of protection via fragments of SEQ ID NO: 1 made up of amino acids 82-486, amino acids 42-196, and amino acids 461-609 of the full-length SEQ ID NO: 2 at second full paragraph on page 8 of their amendment/remarks filed 08/18/08. This Appellant-demonstrated showing cannot be ignored as 'some unidentified alteration' possibly impacting negatively on the ability of the altered SEQ ID NO: 1 to provide protection, but must be viewed as the prima facie demonstration of correlation of the structure of a polypeptide consisting of an amino acid sequence 91% identical to SEQ ID NO: 1 having specifically identified alterations therein, to the **lack** of protection against S. aureus. This is indicative of the lack of strong expectation for SEQ ID NO: 1 having specifically identified alterations therein to remain protective against homologous or heterologous S. aureus. This provides further evidence for the lack of a single, let alone more than one, B-cell and/or T-cell protective epitopes within sufficiently lengthy fragments of SEQ ID NO: 1. Based on this Appellant-established correlation of the altered structure of SEQ ID NO: 1 to the lack of protection, one of skill in the art would not be able to predict 90%, 91%, 92%, 93%, 94%, 95%, 96%. 97%, 98% and 99.0% identical variants of SEQ ID NO: 1 to provide protective immunity against S. aureus in a human or non-human patient or subject. Furthermore, since the second fragment of SEQ ID NO: 1, fragment 3, covering the portions of SEQ ID NO: 1 not covered by fragment 2 plus the amino terminal portion of fragment 3, i.e., amino acids 2-154 of SEQ ID NO: 1, was also correlated by Appellants to **non-protection**, one of skill in the art cannot envision the specific location of one or more protective epitopes within SEQ ID NO: 1 that must be retained while obtaining 90%, 91%, 92%, 93%, 94%, 95%. 96%. 97%, 98% and 99.0% identical variants of SEQ ID NO: 1 that are protective. The fact that the unmodified SEQ ID NO: 1 when merely split into a very lengthy fragment of amino acids 82-486, or a fragment of amino acids 42-196, looses its protective capacity, is indicative of the presence of potential conformational protective epitopes that require amino acid residues from different parts within SEQ ID NO: 1, which epitopes were neither identified by Appellants within the instant specification, nor were they known in the art at the time of the invention. This showing points to the criticality of retaining all the amino acid residues except the N-terminal methionine of the SEQ ID NO: 1 core sequence intact within the claimed polypeptide fragment in order to retain the requisite function of providing protective immunity against S. aureus. If the result from Figure 1A for fragment 2 is to be extrapolated to a human subject, let alone a generic human patient, there would certainly be no expectation of protection.

From the detailed analysis reproduced above and when not taken out of context, one of skill in the art of vaccines and protective efficacy readily understands that a purified polypeptide consisting of SEQ ID NO: 1 induced protection whereas the longer polypeptide of SEQ ID NO: 28 induced approximately 80% death among immunized mice following a challenge infection with an isolate of S. aureus.

In sum, Applicants have failed to identify a single protective epitope within any region along the length of SEQ ID NO: 1, let alone its equivalent region from full length polypeptides of Figures 2A-2E, for one of skill in the art to recognize that Applicants were is possession of the full scope of the claims.

Applicants further criticize the Office's analysis of the scope of the claim limitation 'patient is a human'. As set forth previously, the limitation 'patient is a human' in claims 38, 40, 42 and 44 does not exclude, but includes all human patients including immune-sufficient, immune-deficient, immunocompromised, and immunosuppressed human patients, including cancer patients, AIDS patients, patients with organ transplantation, and patients with end-stage kidney disease etc., among whom multiple drug-resistant and vancomycin-resistant S. aureus infections are known to cause increased mortality and morbidity. The limitation 'patient is a human' also includes neonates, infants, pediatric and geriatric patients as well. Claims 1 and 8 fail to identify the subject, the patient, or the host species, in whom the claimed product provides protective immunity against S. aureus, and therefore the generic limitation 'provides protective immunity against S. aureus' includes providing such protective immunity to any host species, such as vertebrate and non-vertebrate animal species, human and non-human subject and patient species, including all those identified above. All of the above-identified human host species are very relevant host species, since cancer patients, AIDS patients, patients with organ transplantation, and patients with end-stage kidney disease etc. are well known in the art as being at high risk of suffering from S. aureus infections. The purified polypeptide immunogen genus as claimed, with up to 6% non-identity to SEQ ID NO: 3 and SEQ ID NO: 1 anywhere along their length requires the polypeptide immunogen to 'provide protective immunity against S.

aureus', i.e., protective immunity in any of these host or patient species against any strain, serotype, phage type, toxin type, Spa type, or capsular type of S. aureus, vancomycin-resistant and multiple drug-resistant S. aureus. The generic limitation 'provides protective immunity against S. aureus' does not exclude any host species, any patient species, and any isolate of S. aureus. Likewise, the immunogen genus as claimed in claim 7 with up to 10% non-identity to SEQ ID NO: 1 requires the immunogen to have 'the ability to provide protective immunity' as expressly defined at line 25 of page 2 of Applicant's specification. Not one single polypeptide or immunogen species falling within the scope of the instant claims has been correlated with protective immunity against S. aureus in an immune-sufficient human subject, let alone a generic human patient.

Applicants continue to dismiss the teachings of Colman P.M. (Research Immunol. 145:33-36, 1994, of record), McGuiness et al. (Mol. Microbiol. 7:505-514, Feb 1993, of record), and McGuiness et al. (Lancet 337:514-517, March 1991, of record) that were cited in the rejection as being very relevant to the issue of art-recognized unpredictability associated with one or more amino acid alterations within a polypeptide, and continue to allege that the Office has failed to provide sufficient rationale and evidence. Applicants have failed to advance any arguments to address the art-recognized unpredictability documented via the teachings of these references. Without addressing the teachings of these references cited as a part of the rejection and without establishing a structure-function correlation for a representative number of the polypeptide variants encompassed within the scope of the claims, one cannot speculate that polypeptide variants having a high degree of structural similarity are expected to have similar properties. For an altered polypeptide to be protective, it has to minimally bind

immunospecifically with a protective antibody specific to the native polypeptide. Therefore, interaction between a protein and its specific antibody is very relevant for immunospecific protection. As set forth previously, the state of the art documents that a change of even a single amino acid residue can alter the folding of a polypeptide such that the antibody-binding region no longer recognizes the polypeptide. See right column on page 33 of Colman PM. Research Immunol. 145: 33-36, 1994, of record. Without such immunospecific recognition, there cannot be any immunoprotection. It is recognized in the art that even a very conservative substitution may abolish binding. See first full paragraph on page 35 of Colman. Colman further taught that binding interactions could be considered less tolerant because the changes involved occur in what might be called the active site. See third full paragraph on page 35 of Colman. In an unpredictable art, adequate written description of a genus embracing widely variant species cannot be achieved by disclosing one species within the genus, but through sufficient description of a representative number of species within the claimed genus. In the instant case, as set forth previously, the precise structure of a representative number of variant species of SEQ ID NO: 3 and SEQ ID NO: 1 with up to 25 amino acid alterations within SEQ ID NO: 1 as claimed, has not been correlated with the requisite function, i.e., induction of protective immunity against any strain of S. aureus in any host or human patient species. The protein-antibody interaction is minimally needed for immunospecific protection since the antibodies induced by the polypeptide variants are required to first recognize the native polypeptide on pathogenic S. aureus cells and then confer protection against pathogenic S. aureus. Without a structure-function correlation and without the identification of one or more domains, or contiguous or discontiguous epitopes, linear or conformational

epitopes responsible for providing protective immunity against a homologous or heterologous S. aureus in any host species, one of skill in the art would not recognize that inventors had possession of the full scope of the invention as claimed at the time of the invention. The specification fails to teach the structure or precise relevant identifying characteristics of a representative number of such altered polypeptide species sufficient to allow one skilled in the art to determine that inventors had possession of the invention as claimed. Applicants have not described which domains or regions of the recited polypeptide or immunogen variants are correlated with the required capacity to provide such broad protective immunity. Applicants have not described which of SEQ ID NO: 3's and/or SEQ ID NO: 1's amino acids can be varied such that the polypeptide immunogen variant still maintains the capacity to provide such broad protective immunity. The data from Figure 1A definitively demonstrates the lack of protective epitopes in regions within SEQ IS NO: 1 spanning between amino acids 2-41 as well as amino acids 42-446. Without a convincing correlation between structure and function, the claims do little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. Ex parte Kubin, 83 USPQ2d 1410 (Bd. Pat. Appl. & Int. 2007) citing Eli Lilly, 119 F.3d at 1568, 43 USPQ at 1406 ('definition by function ….. does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is').

Clearly, Applicants were not in possession of a representative number of polypeptide fragment species having up to 6% non-identity to SEQ ID NO: 3 and up to 6% non-identity to SEQ ID NO: 1, or a representative number of immunogen species having up to 10% non-identity to SEQ ID NO: 1, and with up to 25 amino acid alterations any where along the length of SEQ ID NO: 1, wherein the species

retain the capacity to provide protective immunity against any generic strain, Spa type, serotype, capsular type, phage type, or clinical isolate of S. aureus in a human or non-human, vertebrate or non-vertebrate patient or subject. As set forth previously, SEQ ID NO: 1 is not sufficiently representative of the claimed broad genus which encompasses 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99.0% identical polypeptide immunogen species capable of providing protective immunity against S. aureus, is the issue. As set forth previously, a protective polypeptide immunogen consisting of an amino acid sequence that is 100% identical to SEQ ID NO: 1 and differing from SEQ ID NO: 1 by having zero amino acid alteration alone is not and cannot be representative of the full scope of the instant claims, but is representative only of one protective polypeptide immunogen species within the claimed broad genus that consists of an amino acid sequence with no amino acid alterations within SEQ ID NO: 1. The Written Description Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus.

The Written Description Guidelines state [Emphasis added]:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is **a well-established correlation** between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

In Enzo Biochem. Inc. v. Gen-Probe Inc., 323 F3.d 956, 964, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002), the Federal Circuit adopted a portion of the Guidelines proffered by the United States Patent and Trademark Office (USPTO). The written

description requirement can be met by describing the claimed subject matter to a person skilled in the art using sufficiently detailed, relevant identifying characteristics such as functional characteristics, and correlating those functional characteristics with a disclosed structure. See Enzo Biochem v. Gen-Probe, 323 F.3d 956, 964, 967, 968 (Fed. Cir. 2002). Sufficient description to show possession of a genus may be achieved by means of disclosure of a representative number of sequence species, defined by sequences falling within the scope of the genus, or recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See University of Rochester, 358 F.3d at 927, 69 USPQ2d at 1895. Clearly, as of the filing date sought, Applicants were not in possession of the full scope 'of the invention'.

Applicants allege that the Office fails to consider all the data provided in the application. However, all mouse survival or lack thereof from each of Figures 1A, 3, 4 and 10 have been fully considered by the Office. Figures 1B-1D and Figures 2A-2E have nothing to do with homologous or hetereologous protection against S. aureus.

The alleged identification of the ORF0657nI region as sufficient to generate an immune response is insufficient. Not one single protective epitope or its precise location has been identified within any of the sequences from Figures 2A-2E or within their SEQ ID NO: 1-equivalent regions, such that one of skill in the art could avoid making up to 25 amino acid alterations therein while obtaining at least 94% or at least 90% identical polypeptide or immunogen variants claimed.

With regard to Applicants' remarks on the undisclosed full length sequence of the Becker strain of S. aureus, the following must be noted. Appellants have previously acknowledged the Office's documentation that the structure or the amino acid sequence of the Becker strain of S. aureus was **not** disclosed in the instant application at the time of filing. Appellants have acknowledged the telephonic conversation that took place between Appellants' representative Mr. Sheldon Heber and the Examiner of record, wherein attorney Sheldon Heber indicated that the Becker ORF0657n sequence is **not** a part of the instant application, and that the Becker sequence was **not** provided in the as filed application. Clearly, the structure of a polypeptide or an immunogen consisting of the SEQ ID NO: 1-equivalent region of the Becker sequence having at least 94% identity with SEQ ID NO: 3 and SEQ ID NO: 1 with up to 25 unspecified or undefined amino acid alterations therein and concurrently having the capacity to provide protective immunity against a laboratory strain or a clinical isolate of S. aureus in an animal or human subject, let alone a generic human patient, was neither in Applicants' possession at the time of the invention, nor was it identified and disclosed within the as-filed specification. The animals of the experiment from Example 3 were <u>not</u> immunized with a polypeptide or an immunogen consisting of the SEQ ID NO: 1-equivalent region of the Becker sequence having at least 94% identity with SEQ ID NO: 3 and SEQ ID NO: 1 with up to 25 unspecified amino acid alterations, or having at least 90% identity with SEQ ID NO: 1 with up to 25 unspecified amino acid alterations therein, before challenge infection with the Becker strain. None of the animals whose survival data at the end of the experiment are to be considered in Figures 1A, 3, 4 and 10 were immunized with a polypeptide or an immunogen consisting of the SEQ ID NO: 1-

equivalent region of the Becker sequence having at least 94% identity with SEQ ID NO: 3 and SEQ ID NO: 1 with up to 25 unspecified amino acid alterations therein, or having at least 90% identity with SEQ ID NO: 1 with up to 25 unspecified amino acid alterations therein. With the express acknowledgment by Applicants that the Becker sequence was not a part of the as-filed specification, one of skill in the art at the time of the invention, could not have envisioned the precise structure of the Becker sequence, let alone SEQ ID NO: 1-equivalent sequence contained therein having the capacity to provide protective immunity against S. aureus.

As set froth previously, the Office documented that a lengthy polypeptide fragment of SEQ ID NO: 1 consisting of most of the length of SEQ ID NO: 1, i.e., amino acids 42-446 of SEQ ID NO: 1 and lacking only amino acids 1-41 of SEQ ID NO: 1, failed to provide protection against S. aureus as demonstrated via 'Fragment 2' in Figure 1A. Applicants continue to assert incorrectly that such a fragment is excluded from claim 7. As explained supra, this fragment is 91% identical to SEQ ID NO: 1 with zero amino acid alterations and certainly falls within the scope of claim 7. Applicants further state that the application provides guidance that N-terminal 40 amino acids from SEQ ID NO: 1 should not be removed, but fail to point to specific portions of the as-filed specification which provide such alleged guidance. To the contrary, Figure 1 clearly demonstrates that a polypeptide fragment that retains the N-terminal 40 amino acids of SEQ ID NO: 1 except the first methionine also **failed** to provide protection against S. aureus. See 'Fragment 3' in Figure 1A. Thus, with regard to the criticality of a specific amino acid sequence or structure, the Office has brought to Applicants' attention the demonstrated evidence from within Applicants' own specification.

Applicants note the Office's documentation of inconsistent and non-reproducible protection demonstrated in the specification, for example, with SEQ ID NO: 4, yet allege that different data in the application have not been considered. It appears as though Applicants want the Office to ignore almost the same level of survival induced by SEQ ID NO: 4 in mice immunized therewith as the one induced in control mice by the AHP adjuvant alone. The alleged protection depicted in Figure 3B does not appear to be immunospecific to SEQ ID NO: 4 since the AHP adjuvant was also able to induce almost the same level of survival. Even if one ignores data from Figure 3B and gives importance to the data depicted in Figure 10 alone, as set forth previously, it demonstrates that it is critical for the claimed sequence species to have at least 99.8% sequence identity to SEQ ID NO: 1 and **not** to have any amino acid alterations along the length of SEQ ID NO: 1 except a single N-terminal amino acid addition after its first methionine, in order to confer about 42% protection against a laboratory strain of S. aureus in an immune-sufficient animal model. The ability of SEQ ID NO: 3 to provide similar degree of protective immunity against S. aureus strain Becker when administered with an adjuvant (see Figure 10) demonstrates that a purified immunogen consisting of an amino acid sequence 100% identical to SEQ ID NO: 1 and having additional more than 20 amino acids from within SEQ ID NO: 2 at the carboxyl terminus of SEQ ID NO: 1, is protective against a laboratory strain of S. aureus in an immune-sufficient animal model. Note that the additional 20 amino acids as recited, for example, in claims 47 and 53 are not required to be from within SEQ ID NO: 2 and can be any 20 amino acids from any source. SEQ ID NO: 3 is <u>not</u> a fragment of SEQ ID NO: 3 or an at least 94% identical sequence thereof as required by claims 1 and 8. SEQ ID NOs: 3, 4 and 5 species are **not** sufficiently representative of the

full scope of the claimed vast genus that encompasses therein polypeptide immunogen fragment variants having 94%, 95%, 96%, 97%, 98% or 99.0% identity to SEQ ID NO: 3, wherein said fragment variants comprise an amino acid sequence having 94%, 95%, 96%, 97%, 98% or 99.0% identity to SEQ ID NO: 1 and differing from SEQ ID NO: 1 by up to 5, 10, or 25 amino acid alterations, including such alterations in non-N-terminal regions of SEQ ID NO: 1. These three species are also not sufficiently representative of the claimed broad genus encompassing immunogen species having 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99.0% sequence identity to an amino acid sequence consisting of SEQ ID NO: 1 and differing from SEQ ID NO: 1 by up to 5, 10, or 25 amino acid alterations including such alterations in non-N-terminal regions of SEQ ID NO: 1. Furthermore, it is important to note that SEQ ID NO: 4, even when administered with the AHP adjuvant, did not provide protection against S. aureus in an immune-sufficient mouse model that was statistically significant compared to the protection conferred by the AHP adjuvant alone in control mice. See Figure 3B. This inconsistent and non-reproducible protection was documented in the Examiners' Answer to highlight the issue of protective unpredictability.

It must be noted that the scope of the instantly claimed genus is not limited to a single polypeptide or immunogen species consisting of an amino acid sequence 100% identical to SEQ ID NO: 1 with no amino acid alterations therein, or to a 99.8% identical variant species containing a single amino acid alteration exclusively after the N-terminal methionine of SEQ ID NO: 1. Instead, the claimed broad genus collectively encompasses a huge number of polypeptide fragment variant species or immunogen fragment variant species consisting of an amino acid sequence that is:

(1) 90% identical to SEQ ID NO: 1;

(2) 91% identical to SEQ ID NO: 1;

(3) 92% identical to SEQ ID NO: 1;

(4) 93% identical to SEQ ID NO: 1;

(5) 94% identical to SEQ ID NO: 1;

(6) 95% identical to SEQ ID NO: 1;

(7) 96% identical to SEQ ID NO: 1;

(8) 97% identical to SEQ ID NO: 1;

(9) 98% identical to SEQ ID NO: 1; and

(10) 99.0% identical to SEQ ID NO: 1,

and differing from SEQ ID NO: 1 by up to 5, 10 and 25 amino acid alterations, wherein the encompassed polypeptide variant species as recited and the immunogen variant species as required by definition, are required to provide protective immunity against homologous or heterologous S. aureus in a human or non-human patient or subject. Thus, the instant claims encompass a vast genus of polypeptide immunogen variants that are fragment variants of SEQ ID NO: 3 and are further variants of SEQ ID NO: 1, having up to 6% non-identity to SEQ ID NO: 3 and SEQ ID NO: 1 (claims 1 and 8), and a vast genus of immunogen variants with up to 10% non-identity to SEQ ID NO: 1 (claim 7), and differing from SEQ ID NO: 1 by up to 5, 10 or 25 amino acid alterations, each having the requisite ability to provide protective immunity against S. aureus. Any amino acids along the length of SEQ ID NO: 3 and/or SEQ ID NO: 1 including the non-amino terminal regions, may be substituted, modified, or deleted as long as the polypeptide fragment retains the percent identity or amino acid alterations as recited. When there is substantial variation within the genus, one must describe a

sufficient variety of species to reflect the variation within the genus. The disclosure of species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure 'indicates that the patentee has invented species sufficient to constitute the gen[us].' See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004) ("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated.").

Applicants' arguments have been carefully considered, but are not persuasive.

Relevant Art

13) A sequence search performed at the Office confirms that the SasJ48-477 polypeptide of a full-length SasJ protein is at least 94% identical with the instantly claimed SEQ ID NO: 3 and SEQ ID NO: 1. The sequence alignments of a

fragment consisting of the amino acid residues 48-477 of the SasJ sequence, SEQ ID NO: 6, for example from US 20080050361A1, and the amino acid residues 48-477 of the SasJ sequence, SEQ ID NO: 12, for example from US 20090317421, with the instantly claimed SEQ ID NO: 3 and SEQ ID NO: 1, are provided below:

(A) The SasJ polypeptide of SEQ ID NO: 6 from US 20080050361A1 is 99.1% identical with the instantly claimed SEQ ID NO: 3. See sequence alignment below.

Instant SEQ ID NO: 3 versus SEQ ID NO: 6 from US 11-740128 (US 20080050361A1):

```
Query Match 99.1%; Score 2279; DB 1; Length 645; Best Local Similarity 99.1%;
Pred. No. 0; Matches 441; Conservative 2; Mismatches 2; Indels 0;  Gaps   0.

Qy         42 SNKEVEAPTSETKEAKEVKEVKAPKETKEVKPAAKATNNTYPILNQELREAIKNPAIKDK 101
              |||||||||||||||||||||||||| |||||||||||||||||||||||||||||||||
Db         82 SNKEVEAPTSETKEAKEVKEVKAPKETKAVKPAAKATNNTYPILNQELREAIKNPAIKDK 141

Qy        102 DHSAPNSRPIDFEMKKKDGTQQFYHYASSVKPARVIFTDSKPEIELGLQSGQFWRKFEVY 161
              |||||||||||||||::| |||||||||||||||||||||||||||||||||||||||||
Db        142 DHSAPNSRPIDFEMKKENGEQQFYHYASSVKPARVIFTDSKPEIELGLQSGQFWRKFEVY 201

Qy        162 EGDKKLPIKLVSYDTVKDYAYIRFSVSNGTKAVKIVSSTHFNNKEEKYDYTLMEFAQPIY 221
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        202 EGDKKLPIKLVSYDTVKDYAYIRFSVSNGTKAVKIVSSTHFNNKEEKYDYTLMEFAQPIY 261

Qy        222 NSADKFKTEEDYKAEKLLAPYKKAKTLERQVYELNKIQDKLPEKLKAEYKKKLEDTKKAL 281
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        262 NSADKFKTEEDYKAEKLLAPYKKAKTLERQVYELNKIQDKLPEKLKAEYKKKLEDTKKAL 321

Qy        282 DEQVKSAITEFQNVQPTNEKMTDLQDTKYVVYESVENNESMMDTFVKHPIKTGMLNGKKY 341
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        322 DEQVKSAITEFQNVQPTNEKMTDLQDTKYVVYESVENNESMMDTFVKHPIKTGMLNGKKY 381

Qy        342 MVMETTNDDYWKDFMVEGQRVRTISKDAKNNTRTIIFPYVEGKTLYDAIVKVHVKTIDYD 401
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        382 MVMETTNDDYWKDFMVEGQRVRTISKDAKNNTRTIIFPYVEGKTLYDAIVKVHVKTIDYD 441

Qy        402 GQYHVRIVDKEAFTKANTDKSNKKEQQDNSAKKEATPATPSKPTPSPVEKESQKQDSQKD 461
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        442 GQYHVRIVDKEAFTKANTDKSNKKEQQDNSAKKEATPATPSKPTPSPVEKESQKQDSQKD 501

Qy        462 DNKQLPSVEKENDASSESGKDKTPA 486
              |||||||||||||||||||||||||
Db        502 DNKQLPSVEKENDASSESGKDKTPA 526
```

Roche's purified fragment consisting of the amino acid residues 48-477 of this SasJ sequence, SEQ ID NO: 6, is at least 95.3% identical to the instantly claimed SEQ ID NO: 1. See the sequence alignment below.

Instant SEQ ID NO: 1 versus SEQ ID NO: 6 from US 11-740128 (US 20080050361A1):

```
Query Match 95.3%; Score 2193; DB 1; Length 430; Best Local Similarity 99.1%;
Pred. No. 0; Matches 426; Conservative 2; Mismatches 2; Indels 0;  Gaps  0.

Qy          8 TNTEAQPKTEAVASPTTTSEKAPETKPVANAVSVSNKEVEAPTSETKEAKEVKEVKAPKE 67
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 TNTEAQPKTEAVASPTTTSEKAPETKPVANAVSVSNKEVEAPTSETKEAKEVKEVKAPKE 60

Qy         68 TKEVKPAAKATNNTYPILNQELREAIKNPAIKDKDHSAPNSRPIDFEMKKKDGTQQFYHY 127
              || |||||||||||||||||||||||||||||||||||||||||::| ||||||
Db         61 TKAVKPAAKATNNTYPILNQELREAIKNPAIKDKDHSAPNSRPIDFEMKKENGEQQFYHY 120

Qy        128 ASSVKPARVIFTDSKPEIELGLQSGQFWRKFEVYEGDKKLPIKLVSYDTVKDYAYIRFSV 187
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 ASSVKPARVIFTDSKPEIELGLQSGQFWRKFEVYEGDKKLPIKLVSYDTVKDYAYIRFSV 180

Qy        188 SNGTKAVKIVSSTHFNNKEEKYDYTLMEFAQPIYNSADKFKTEEDYKAEKLLAPYKKAKT 247
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 SNGTKAVKIVSSTHFNNKEEKYDYTLMEFAQPIYNSADKFKTEEDYKAEKLLAPYKKAKT 240

Qy        248 LERQVYELNKIQDKLPEKLKAEYKKKLEDTKKALDEQVKSAITEFQNVQPTNEKMTDLQD 307
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 LERQVYELNKIQDKLPEKLKAEYKKKLEDTKKALDEQVKSAITEFQNVQPTNEKMTDLQD 300

Qy        308 TKYVVYESVENNESMMDTFVKHPIKTGMLNGKKYMVMETTNDDYWKDFMVEGQRVRTISK 367
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 TKYVVYESVENNESMMDTFVKHPIKTGMLNGKKYMVMETTNDDYWKDFMVEGQRVRTISK 360

Qy        368 DAKNNTRTIIFPYVEGKTLYDAIVKVHVKTIDYDGQYHVRIVDKEAFTKANTDKSNKKEQ 427
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 DAKNNTRTIIFPYVEGKTLYDAIVKVHVKTIDYDGQYHVRIVDKEAFTKANTDKSNKKEQ 420

Qy        428 QDNSAKKEAT 437
              ||||||||||
Db        421 QDNSAKKEAT 430
```

(B) Similarly, the SasJ polypeptide of SEQ ID NO: 12 from US 20090317421 is 99.1% identical with the instantly claimed SEQ ID NO: 3. See sequence alignment below.

Instant SEQ ID NO: 3 versus SEQ ID NO: 12 from US 12-161315 (US 20090317421):

```
US-12-161-315-12
Sequence 12, Application US/12161315
Publication No. US20090317421A1
GENERAL INFORMATION
APPLICANT: MISSIAKAS, DOMINIQUE
APPLICANT:STRANGER-JONES, YUKIKO
APPLICANT:BURTS, MONICA
APPLICANT:SCHNEEWIND, OLAF
TITLE OF INVENTION: COMPOSITIONS AND METHODS RELATED TO STAPHYLOCOCCAL
TITLE OF INVENTION:BACTERIUM PROTEINS
FILE REFERENCE: ARCD:430US
CURRENT APPLICATION NUMBER: US/12/161,315
CURRENT FILING DATE: 2008-07-17
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PRIOR APPLICATION NUMBER: PCT/US2007/060720
PRIOR FILING DATE: 2007-01-18
PRIOR APPLICATION NUMBER: 60/841,52
PRIOR FILING DATE: 2006-08-31
PRIOR APPLICATION NUMBER: 60/760,008
PRIOR FILING DATE: 2006-08-18
NUMBER OF SEQ ID NOS: 56
SOFTWARE: PatentIn Ver. 2.1
SEQ ID NO 12
LENGTH: 645
TYPE: PRT
ORGANISM: Staphylococcus sp.
US-12-161-315-12

Query Match 99.1%; Score 2890; DB 8; Length 645; Best Local Similarity 99.3%;
Matches 564; Conservative 2; Mismatches 2; Indels 0; Gaps 0.

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Qy          2 AEETGGTNTEAQPKTEAVASPTTTSEKAPETKPVANAVSVSNKEVEAPTSETKEAKEVKE 61
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         42 AEETGGTNTEAQPKTEAVASPTTTSEKAPETKPVANAVSVSNKEVEAPTSETKEAKEVKE 101

Qy         62 VKAPKETKEVKPAAKATNNTYPILNQELREAIKNPAIKDKDHSAPNSRPIDFEMKKKDGT 121
              |||||||| ||||||||||||||||||||||||||||||||||||||||||||||::||
Db        102 VKAPKETKAVKPAAKATNNTYPILNQELREAIKNPAIKDKDHSAPNSRPIDFEMKKENGE 161

Qy        122 QQFYHYASSVKPARVIFTDSKPEIELGLQSGQFWRKFEVYEGDKKLPIKLVSYDTVKDYA 181
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        162 QQFYHYASSVKPARVIFTDSKPEIELGLQSGQFWRKFEVYEGDKKLPIKLVSYDTVKDYA 221

Qy        182 YIRFSVSNGTKAVKIVSSTHFNNKEEKYDYTLMEFAQPIYNSADKFKTEEDYKAEKLLAP 241
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        222 YIRFSVSNGTKAVKIVSSTHFNNKEEKYDYTLMEFAQPIYNSADKFKTEEDYKAEKLLAP 281

Qy        242 YKKAKTLERQVYELNKIQDKLPEKLKAEYKKKLEDTKKALDEQVKSAITEFQNVQPTNEK 301
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        282 YKKAKTLERQVYELNKIQDKLPEKLKAEYKKKLEDTKKALDEQVKSAITEFQNVQPTNEK 341

Qy        302 MTDLQDTKYVVYESVENNESMMDTFVKHPIKTGMLNGKKYMVMETTNDDYWKDFMVEGQR 361
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        342 MTDLQDTKYVVYESVENNESMMDTFVKHPIKTGMLNGKKYMVMETTNDDYWKDFMVEGQR 401

Qy        362 VRTISKDAKNNTRTIIFPYVEGKTLYDAIVKVHVKTIDYDGQYHVRIVDKEAFTKANTDK 421
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        402 VRTISKDAKNNTRTIIFPYVEGKTLYDAIVKVHVKTIDYDGQYHVRIVDKEAFTKANTDK 461

Qy        422 SNKKEQQDNSAKKEATPATPSKPTPSPVEKESQKQDSQKDDNKQLPSVEKENDASSESGK 481
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        462 SNKKEQQDNSAKKEATPATPSKPTPSPVEKESQKQDSQKDDNKQLPSVEKENDASSESGK 521

Qy        482 DKTPATKPTKGEVESSSTTPTKVVSTTQNVAKPTTASSKTTKDVVQTSAGSSEAKDSAPL 541
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        522 DKTPATKPTKGEVESSSTTPTKVVSTTQNVAKPTTASSKTTKDVVQTSAGSSEAKDSAPL 581

Qy        542 QKANIKNTNDGHTQSQNNKNTQENKAKS 569
              ||||||||||||||||||||||||||||
Db        582 QKANIKNTNDGHTQSQNNKNTQENKAKS 609
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Roche's purified fragment consisting of the amino acid residues 48-477 of this SasJ sequence, SEQ ID NO: 12, is at least 95.3% identical to the instantly claimed SEQ ID NO: 1. See the sequence alignment below.

Instant SEQ ID NO: 1 versus SEQ ID NO: 12 from US 12-161315 (US 20090317421):

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us-12-161-315-12

 Query Match 95.3%; Score 2193; DB 1; Length 430; Best Local Similarity 99.1%;
 Pred. No. 0; Matches 426; Conservative 2; Mismatches 2; Indels 0; Gaps  0.

Qy          8 TNTEAQPKTEAVASPTTTSEKAPETKPVANAVSVSNKEVEAPTSETKEAKEVKEVKAPKE 67
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 TNTEAQPKTEAVASPTTTSEKAPETKPVANAVSVSNKEVEAPTSETKEAKEVKEVKAPKE 60

Qy         68 TKEVKPAAKATNNTYPILNQELREAIKNPAIKDKDHSAPNSRPIDFEMKKKDGTQQFYHY 127
              || |||||||||||||||||||||||||||||||||||||||||::| ||||||
Db         61 TKAVKPAAKATNNTYPILNQELREAIKNPAIKDKDHSAPNSRPIDFEMKKENGEQQFYHY 120

Qy        128 ASSVKPARVIFTDSKPEIELGLQSGQFWRKFEVYEGDKKLPIKLVSYDTVKDYAYIRFSV 187
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 ASSVKPARVIFTDSKPEIELGLQSGQFWRKFEVYEGDKKLPIKLVSYDTVKDYAYIRFSV 180

Qy        188 SNGTKAVKIVSSTHFNNKEEKYDYTLMEFAQPIYNSADKFKTEEDYKAEKLLAPYKKAKT 247
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 SNGTKAVKIVSSTHFNNKEEKYDYTLMEFAQPIYNSADKFKTEEDYKAEKLLAPYKKAKT 240

Qy        248 LERQVYELNKIQDKLPEKLKAEYKKKLEDTKKALDEQVKSAITEFQNVQPTNEKMTDLQD 307
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 LERQVYELNKIQDKLPEKLKAEYKKKLEDTKKALDEQVKSAITEFQNVQPTNEKMTDLQD 300

Qy        308 TKYVVYESVENNESMMDTFVKHPIKTGMLNGKKYMVMETTNDDYWKDFMVEGQRVRTISK 367
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 TKYVVYESVENNESMMDTFVKHPIKTGMLNGKKYMVMETTNDDYWKDFMVEGQRVRTISK 360

Qy        368 DAKNNTRTIIFPYVEGKTLYDAIVKVHVKTIDYDGQYHVRIVDKEAFTKANTDKSNKKEQ 427
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 DAKNNTRTIIFPYVEGKTLYDAIVKVHVKTIDYDGQYHVRIVDKEAFTKANTDKSNKKEQ 420

Qy        428 QDNSAKKEAT 437
              ||||||||||
Db        421 QDNSAKKEAT 430
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14) The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- With regard to the structure-function relationship of an encoded amino acid sequence in general, Rudinger et al. (In: Peptide Hormones. (Ed) JA Parsons, University Park Press, pages 1-7, June 1976) taught that 'the significance of particular amino acid sequences for different aspects of biological activity cannot

be predicted a priori but must be determined from case to case by painstaking experimental study'. See page 6. Rudinger et al. further taught that 'it is impossible to attach a unique significance to any residue in a sequence' and that a 'given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence. See page 3.

- The state of the art reflects unpredictability as to which amino acids in a specific protein can be varied, i.e., replaced or added, without adversely affecting the functional properties of that specific protein. In other words, the retention of the immunospecificity following one or more amino acid substitutions, including conservative amino acid substitutions within a bacterial polypeptide is not predictable. For instance:

(A) McGuinnes et al. (Mol. Microbiol. 7: 505-514, 1993, of record) taught that "[a] single amino acid change within an epitope, or an amino acid deletion outside an epitope, were both associated with loss of subtype specificity resulting from a change in the predicted conformation at the apex of the loop structure" in case of a meningococcal polypeptide. See abstract.

(B) Similarly, (B) McGuinnes et al. (Lancet 337: 514-517, March 1991, of record) taught that a point mutation generating a single amino acid change in a P1.16-specific epitope in the VR2 region of the porA gene of a strain of Neisseria meningitidis of subtype P1.7,16 resulted in "striking changes in the structural and immunological properties of the class 1 protein" of this isolate. See abstract and page 514.

- US 2006-0177462 A1 documents the functional unpredictability associated with variants of staphylococcal polypeptides. For example, a purified

polypeptide immunogen consisting of SEQ ID NO: 1, which is a truncated full length ORF0657n polypeptide (SEQ ID NO. 2) of S. aureus COL, is shown to be protective against a strain of S. aureus. See Figure 1A. However, a polypeptide variant consisting of an amino acid sequence that is 90.58% identical to said SEQ ID NO: 1, depicted as fragment 2 in Figure 1A via one of the open rectangles, was found **not** to be protective. See paragraph [0032]. This is indicative of unpredictability in obtaining a polypeptide species that is about 10% non-identical in structure to SEQ ID NO: 1 and that remains protective against S. aureus infection. Furthermore, paragraph [0047] states that a fragment of SEQ ID NO: 2 consisting of amino acids 82-486 or amino acids 42-196 was **not** protective. This documented non-protection by the fragments of SEQ ID NO: 2 or 1 consisting of amino acids 82-486 or amino acids 42-196, with zero amino acid alterations therein, appears to indicate the absence of one or more protective epitopes in these regions. Thus, the unmodified SEQ ID NO: 1 when merely split into a fragment of amino acids 82-486, or amino acids 42-196, looses its protective capacity, indicating the criticality of retaining all the amino acid residues of SEQ ID NO: 1 intact within the claimed fragment/variant in order to retain the requisite function of providing protective immunity against S. aureus. Thus, there is a demonstrated lack of predictability as to whether polypeptide variants having up to 10% non-identity to SEQ ID NO: 1 anywhere along SEQ ID NO: 1 would remain immunospecific to S. aureus and provide protective immunity against S. aureus in a human or a non-human host or patient.

- It is well established in the art that immunogenicity/antigenicity does not correlate with protection from infection. Chandrashekar et al (US Patent 6,248,329) taught '... it is well understood that the ability of an antigen to stimulate

antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection..'. See column 1, lines 35-42.

- Greenspan et al. (Nature Biotechnology 7: 936-937, 1999) taught that defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope". According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. See page 937, column 2.

- Skolnick et al. (Trends in Biotechnology 18: 34-39, 2000) taught that a skilled artisan is well aware that assigning functional activities for any particular protein or a family of proteins based upon sequence homology is inaccurate, partly because of the multifunctional nature of proteins. See abstract and page 34. Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein. See abstract and Box 2.

- While it is known in the art that variation in one or more amino acids is possible in a given protein, the exact position within its amino acid sequence where replacements or variations can be made, with a reasonable expectation of success of retaining the protein's functional integrity, is not certain. A random replacement affecting the epitopic amino acid positions that are critical, for example, to the three-dimensional conformational structure and specific binding

property of the protein, would result in a polypeptide that may be non-functional (i.e., non-immunogenic) or not optimally immunogenic or protective as a vaccine candidate, because such positions tolerate no or little modifications. For example, Houghten et al. (New Approaches to Immunization, Vaccines86, Cold Spring Harbor Laboratory, p. 21-25, 1986) teach the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten et al. state (see page 24) [Emphasis added]:

> One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively **unrecognizable** by any of the antibodies in the polyclonal pool.

Thus, the art reflects that variations in critical residues at specific positions in an amino acid sequence could result in a polypeptide which may induce an antibody that may not recognize or bind to the native polypeptide of a microorganism.

Remarks

15) Claims 1, 4, 7-9, 33-35 and 38-54 stand rejected.

Claims 5, 6 and 36 stand objected to as indicated previously.

16) Applicants' submission of an information disclosure statement under 37 CFR 1.97 with the fee set forth in 37 CFR 1.17(p) on 01/20/11 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened

statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

18) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

19) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

/S. Devi/ April, 2011
Primary Examiner, AU 1645

/Gary B. Nickol /

Supervisory Patent Examiner, Art Unit 1645